PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BOULT WADE TENNANT
Verulam Gardens
70 Gray's Inn Road
London WC1X 8BT
ROYAUME-UNI

Date of mailing (day/month/year)
02 May 2000 (02.05.00)

Applicant's or agent's file reference
SCB/50965001

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/02241

International filing date (day/month/year)
14 July 1999 (14.07.99)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address
BOULT WADE TENNANT
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2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
BOULT WADE TENNANT
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3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[X] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
Maria Victoria CORTIELLO
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 14 February 2000 (14.02.00)	
International application No. PCT/GB99/02241	**Applicant's or agent's file reference** SCB/50965001
International filing date (day/month/year) 14 July 1999 (14.07.99)	**Priority date** (day/month/year) 14 July 1998 (14.07.98)
Applicant PANGALOS, Menlas et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

18 January 2000 (18.01.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Jean-Marc Vivet
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BOULT WADE TENNANT
VERULAM GARDENS
70 Gray's Inn Road
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GRANDE BRETAGNE

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	03.08.2000
Applicant's or agent's file reference SCB/50965001	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/02241	14/07/1999	14/07/1998

International Patent Classification (IPC) or both national classification and IPC

C12N15/52

Applicant

JANSSEN PHARMACEUTICA N.V. et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 14/11/2000.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
Wimmer, G

Formalities officer (incl. extension of time limits)
Christensen, J
Telephone No. +49 89 2399 8052

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".)*:

Description, pages:

1-63 as originally filed

Claims, No.:

1-48 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:

see separate sheet

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 5, 7, 9, 10, 12, 15
Inventive step (IS)	Claims	1-48
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

Re Item IV

Lack of unity of invention.

The present patent application refers to three members of the NAALADase group of peptidases. Specifically, full-length human NAALADase-L, and two previously unidentified members of the gene family, termed NAALADase-II and NAALADase IV, were isolated from human cDNA.

The common technical feature (Rule 13.2 PCT) to the genes and proteins subject of the current application, is that they belong to the family of NAALADases.

This feature, however, does not define a contribution over the prior art, since several members of NAALADases were already defined in the prior art (document D1, abstract; document D2, and references therein). Thus, since the common technical feature of the inventions claimed in the application is not inventive, unity of invention is compromized.

The claims of the current application are therefore regarded as referring to three different inventions:

I) human NAALADase-L, Claims 1-4, 10-11, as well as (all partially) 9 and 18-48
II) NAALADase-II, Claims 5-6, 12-14, as well as (all partially) 9 and 18-48
III) NAALADase-IV, Claims 7-8, 15-17, as well as (all partially) 9 and 18-48

Since, however, the examination of these different inventions poses no excessive effort, no invitation to restrict or to pay additional fees is extended at the moment.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability.

The application does not meet the requirements of Art. 33 PCT since **claims 1, 5, 7, 9, 10, 12 and 15 are not novel,** and **claims 1-48 do not appear to contain an inventive step**.

1) Reference is made to the following documents (the document numbering corresponds to their order of citation in the international search report):
   D1: SHNEIDER, B.L., ET AL.: "Cloning and characterization of a novel peptidase from rat and human ileum." J.BIOL.CHEM., vol. 272, no. 49, 5 December 1997, pages 31006-31015, XP002129302
   D2: LUTHI-CARTER R, ET AL.: "Isolation and characterization of a rat brain cDNA encoding glutamate carboxypeptidase II" PROC.NATL.ACAD.SCI. USA, vol. 95, March 1998, pages 3215-3220, XP002129303

2) The scope of **claim 1** extends to a cDNA molecule encoding human NAALADase-L, or a functional equivalent thereof.

   In lack of a precise definition of a function which distinguishes human NAALADase-L from the NAALADases already known in the prior art, a similar function is assumed on the basis of protein homology. Vice versa, the known forms of NAALADase-I (D2, entire document, and references therein), as well as rat NAALADase-L (D1, entire document), can be regarded as functional equivalents of human NAALADase-L.

   Since this is comprised in the subject-matter of claim 1, this claim can not be regarded as being novel.

   The same applies to the related **claim 10**, which refers to the human NAALADase-L protein itself, or a functional equivalent thereof.

3) For the same reasons, the NAALADases known in the prior art can be regarded as functional equivalents of NAALADase-II and NAALADase-IV. Therefore, **claims 5 and 12**, and **claims 7 and 15**, the scope of which extends to functional equivalents of NAALADase-II and NAALADase-IV, respectively, cannot be considered to be novel.

4) However, **claims 2 - 4 and 11**, which refer more specifically to a precise nucleotide or amino acid sequence of human NAALADase-L or splice variants thereof, neither of which have been disclosed entirely in the prior art, can be considered to be novel.

For similar reasoning, **claims 6, 13 and 14**, and **claims 8, 16 and 17**, which refer to specific nucleotide or amino acid sequences of human NAALADase-II and human NAALADase-IV, respectively, are regarded as being novel.

5) Besides the fact that **claim 9** also may depend on the claims 1, 5 and 7, all of which lack novelty, the scope of this claim also lacks a precise definition, since a minimal length of the nucleic acid molecule subject of the claim is not given. It may thus be understood as being limited to a sequence of one or few bases, which have doubtlessy been disclosed in the prior art.
This claim therefore also lacks novelty.

6) Novelty of the **claims 18 - 48** can only be examined if novelty of all claims they depend on has been restored.

Inventive Step.

7) The genes and proteins for human, rat and murine NAALADase-I, and for rat NAALADase-L, were known in the prior art. Also, a cDNA fragment encoding roughly half of human NAALADase-L was described.

The technical problem therefore was the identification of new genes and proteins with similar properties.

The obvious solution to the person skilled in the art would be the identification of genes related to the known NAALADases, by sequence comparison and standard cloning thechniques.

The solution of the present patent application is the provision of human NAALADase-L, human NAALADase-II and human NAALADase-IV.

The identification of the genes was performed by the inventors as follows:

human NAALADase-L:

- With the sequence information from the prior art, PCR primers for the 3' end of human NAALADase-L were designed.
- PCR was performed using commercially available cDNA as template.
- To obtain the 5' end of the gene, a RACE assay was performed using a standard kit.

human NAALADase-II:

- With all sequence informations on NAALADases from the prior art, BLAST searches on EST databases were performed.
- Positive clones were ordered and sequenced. One of them contained an entire reading frame coding for a protein, which was designated NAALADase-II.

human NAALADase-IV:

- Sequence information from another positive EST clone revealed a partial coding sequence of another NAALADase. This sequence was used in a second BLAST comparison to EST databases.
- The resulting sequence information yielded a contig encoding a protein, which was designated NAALADase-IV. Isolation of the entire gene was performed by PCR.

The isolation of these genes has thus clearly been performed by standard methods used in the field, and was based on sequence information of the known

NAALADases.
Since moreover the new NAALADases do not seem to show a surprising effect, the identification and isolation of the genes and proteins therefore lacks an inventive step.

Thus, **claims 1-8** and **10-17**, which refer to the NAALADases subject of the application, and to the nucleic acids encoding said NAALADases, are regarded as not complying with Art. 33(3) PCT.

8) Dependent **claims 9 and 18-48** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.